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DISSEMINATED SYPHILITIC ENCEPHALITIS.

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The following study is of a case of syphilis of the central nervous system, which presents points of interest in its pathological histology and as an example of the occurrence of severe syphilis of the nervous system soon after infection, at a time when the constitutional symptoms were still marked. There occur in the nervous system a variety of lesions, some of which may be regarded as specific; others cannot be differentiated from simple inflammatory phenomena. These inflammatory phenomena occur throughout the entire cortex, and also as focal areas of granulation tissue. These latter so overshadow the other features that it seems best to designate the case one of disseminated syphilitic encephalitis.

Summary of the Clinical History. C. C., male, aged forty-one years, admitted to the Danvers Insane Hospital, December 11, 1902. Family and early personal history not noteworthy. While not a steady drinker, he occasionally used alcohol to excess. June 12, 1902 he consulted a physician, giving a history of syphilitic infection three weeks previous, and then showed an initial lesion on the dorsum of the glans penis. On July 2, he was again seen by the same physician at a time when just recovering from an alcoholic debauch. The primary sore then showed extensive ulceration, and there was a papular eruption over the arms, chest, abdomen and legs. He was put upon a specific treatment of mercury, with occasional weeks of mixed treatment. An attack of iritis occurred, but soon disappeared with increased dosage. In the latter part of November, or about six months after infection, he had severe headaches which could be only partially controlled by treatment. Soon he became forgetful and was described as being "stupid." He was neglectful of his personal habits and "too stupid to eat." This condition led to his commitment to this hospital.

The examination made at his admission by Dr. Mitchell shows that he was poorly nourished, weighing 124 pounds. He was so feeble that he was immediately put in bed. His face was dull and expressionless. He moved restlessly from side to side and made coarse purposeless movements with his arms. A general eruption was present; over the arms and legs this was of more or less discrete scaly papules, over the chest more of a maculopapular type. On the dorsum of the glans penis there was a recent scar. In the mouth were a number of mucous patches. The inguinal and epitrochlear glands were enlarged.

The left pupil was larger than the right. Light reactions could not be tested satisfactorily on account of the patient's restlessness. There was external strabismus of the right eye and partial ptosis of this lid. The knee-jerks were increased and there was a crossed adductor reflex. No ankle clonus. There was coarse tremor of the arms and hands. Tongue steady when protruded. Mentally, he showed extreme clouding of consciousness; only occasionally could his attention be gained and a relevant answer obtained to the question. Disorientation was complete. He was stuporous and frequently dozed during the examination.

December 15*th*. Stupor more marked; he showed coarse restlessness and moved purposelessly about the bed. He passed his urine and feces without control. His attention was obtained only by loud tones, and could not be held.

17*th*. Difficulty in swallowing, the food regurgitating through the nose. Ptosis of right lid more marked; slight external strabismus. Muscular twitchings of the right side.

18*th*. Comatose. Irritation of the left leg produced twitchings of the left leg and arm. Slight spasticity of right arm and leg. Left pupil larger than right; neither reacted to light stimuli. Died on this day.

Autopsy Five and a Half Hours Post-mortem. Male body, aged forty-one years, moderately well developed, but poorly nourished. Post-mortem rigidity is present only in the lower jaw. In the conjunctiva of the inner half of the left eyeball is a diffuse hemorrhage. Scattered over the thorax and abdomen are many yellow-brown scars; most of these measure a few millimetres in diameter, the largest rarely reaching 10 mm. On the arms are numerous papules with scaly tops. On the legs are many pigmented scars similar in appearance to those on the thorax; among these are scattered papules with scaly crusts; around the ankles are similar papules; the skin about these shows several small, scattered areas of ecchymoses.

Heart. Not notable save for a small hemorrhagic focus in the mitral valve.

Lungs. Considerable œdema and hypostasis in the posterior parts. In the left apex is a firm nodule 1 cm. in diameter.

Microscopic Examination. This nodule appears as a caseous substance surrounded by a thick fibrous capsule. Capillaries throughout the section are intensely engorged. In some of the alveoli there are a few polynuclear leukocytes and epithelioid cells; many of these latter have inclusions of pigment granules; fewer have one or two red cells and occasionally a lymphocyte.

Spleen and Kidneys. Not notable.

Liver. Capsule of the left lobe shows a broad, milk-colored patch of thickening. Liver substance considerably engorged.

Microscopic Examination. Sections through the capsule show an increase of connective tissue with infiltration of lymphoid cells between the fibrils. The periportal connective tissue is much increased. Many of the central veins are engorged and the capillaries dilated. The liver cells of the central part of the alveoli frequently show fatty degeneration.

Sections through a papule of the skin of the arm show at one place an infiltration of the stratum corneum with polynuclear leukocytes, otherwise the epidermis is not notable. In the cutis there are places where accumulations of lymphoid and plasma cells and the fixed tissue cells are swollen. The bloodvessels here and in the subcutaneous areolar tissues have their walls crowded with plasma cells. The coil glands are strikingly free from cellular accumulations.

Sections through the glans penis show dense infiltration of the cutis with lymphoid and plasma cells among which are many mast cells. Focal accumulations of these cells lie deep in the tissue of the glans. The other internal organs show nothing unusual.

Cultures from the heart, spleen and meninges were negative.

Head. Calvarium and dura mater not notable. The pia mater of the convexity shows a slight haziness. Over the base, especially below the cisterna and from here spreading out over the pons and into the fissures of Sylvius on both sides, it is thickened, hazy, and hyperæmic. The thickening is most marked around the root of the right third nerve, and here the pia has a grayish, gelatinous appearance. The left middle cerebral artery, in the first part of its length, is considerably thickened.

The brain was sectioned after the method of Meynert, and in the gross showed nothing unusual except a small hemorrhage among the pyramidal fibres of the right side of the pons; here there is one hemorrhagic area about 7 mm. in diameter, around which are numerous small punctiform hemorrhages. The brain weighed 1360 grams. Save for a slight haziness of the pia, the cord showed nothing unusual in gross appearance.

At the autopsy some material for the following histological study was immediately fixed in Zenker's fluid and in alcohol. The remainder of the brain and cord were put into 10 per cent. formalin, and after a few days hardening the other material studied was cut and used for a variety of methods.

The descriptions of the meningitis are chiefly of material taken from the frontal regions and from the pia at the base of the brain fixed in Zenker's fluid and stained with eosin and methylene blue. That of the bloodvessels from similarly prepared sections.

The descriptions of cell changes of the cortex and cord are of alcohol-hardened material taken from the frontal, parietal and calcarine regions and various levels of the cord cut unimbedded and stained according to Nissl's method. Later further material was cut out from the formalin-hardened brain and put into alcohol and then stained in a similar way. The glia fibre studies are of material cut from the brain after a few days in 10 per cent. formalin and stained by Weigert's method; and of material cut the same as for Nissl's method but stained according to Benda's method for neuroglia fibres.

The medullated fibre descriptions are of material cut from the brain and cord after a few days hardening in 10 per cent. formalin and later put into Müller's fluid; afterward sections from these pieces were stained after the modification of Weigert's method described by Schaeffer.

Meninges. The characteristic lesion of the meninges—*i. e.*, the pia-arachnoid, is an infiltration of its meshes with cellular elements and proliferative and degenerative changes in its vessels, or a meningitis. The changes in the pia are so related with those of the vessels which lie in it that they will be considered together.

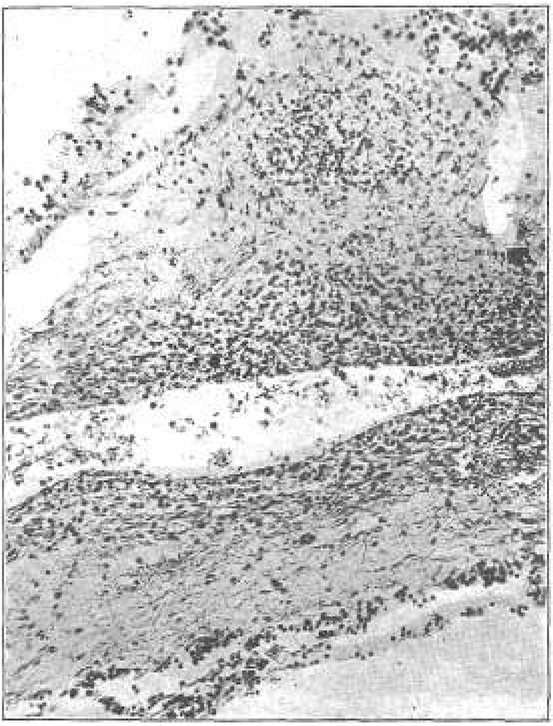
The meningitis shows local variations in its severity and in the character of its elements. In some places the pia appears quite normal; in others the meningitis is very intense. Generally the infiltration increases from a few cells lying in the deepest meshes of the pia to larger accumulations which distend the spaces and produce great thickening of the membrane. The greatest amount of infiltration occurs above and in the sulci. The exudate contains but little fibrin. The largest amount of fibrin, and this only a few threads, lies in an accumulation of polynuclear leukocytes in the region of a necrotic area. Where the exudate is least in quantity it is made up largely of lymphocytes arranged in a row compressed against the underlying cortex; among these are scattered a few plasma cells and occasionally an epithelioid cell, rarely a polynuclear leukocyte.

As the exudate increases in quantity the infiltrating elements spread into the upper meshes of the pia; epithelioid cells are here more common; plasma cells retain about the same relative proportion among the lymphocytes; polynuclear leukocytes are a little more frequently seen. In many places the exudate is so great that its cells lose all row-like arrangement and the meshes of the pia are torn apart; in these places the epithelioid cells not infrequently have inclusions of lymphocytes, usually one, but sometimes as many as six in a single cell.

There are places where focal accumulations of lymphocytes occur.

The exudate is always most abundant around the vessels and in these places shows the greatest variety among its elements. Plasma cells are always most numerous in the adventitia of the veins and here greatly outnumber the lymphocytes. Where the lymphocytes and plasma cells are intermingled, and in the exudate generally, it is possible to find, in sections stained by Unna's pyronin method, granules in the protoplasm of cells which in every other respect resemble lymphocytes; it is often quite difficult to distinguish between plasma cells and lymphocytes.

FIG. 1.



Vein in pia mater with necrotic nodule in the adventitia. Eosin-methylene-blue stain. Magnification 150.

The polynuclear leukocytes vary greatly in their distribution. Where the exudate is present in any considerable quantity they lie scattered at rare intervals. In some places they are in numbers and have a focal arrangement. This occurs in or near areas in which the tissues show necrosis, and is continuous with an infiltration of a vessel wall with leukocytes. There are a number of necrotic foci (Fig. 1); one appears as a knob-like mass projecting from the adventitia of a vein. The media at this point is well stained but infiltrated with polynuclear leukocytes. The adventitia is in a characteristic necrotic state. The cytoplasm of its cellular elements stains poorly, and scattered everywhere through the area are nuclear fragments. Polynuclear leukocytes in various stages of disintegration are numerous. In these places there is a striking absence of lymphoid and epithelioid cells. With bacterial stains it was not possible to find any unquestionable micro-organisms. On the whole, apart from these focal areas where necrosis is present, the polynuclear leukocytes play little part in the meningeal exudate.

Arteries. The arteries of the pia show a variety of changes, the commonest of which is a proliferation of the connective-tissue cells of the intima; with this proliferation there is present an infiltration of the walls of the vessel.

In most instances the proliferation involves only part of the circumference of the intima. In a few arteries it extends completely around the lumen, but is then always of uneven thickness.

Not all of the vessels show changes, the majority appearing quite normal. The location of the arteries showing endarteritis seems to bear no relation to the intensity of the meningitis.

The endarteritis is not always present in those arteries around which the infiltration of the pia is most marked; and on the other hand, some arteries show severe endarteritis where the meningeal infiltration is very slight. The best general picture of the endarteritis is gained in preparations stained by Mallory's connective-tissue method. Normally the arteries of the pia, which are classed as of medium size, when stained by this method appear about as follows: bordering the lumen is a thin layer of blue fibrils, on which are red endothelial cells; this represents the intima, and follows the wavy outline of the underlying elastica, which appears as a homogeneous orange-red layer. Outside of the elastica is the media, with bluish fibrils interlacing among the red-colored muscle elements; external to this is the more or less broad layer of loosely arranged blue fibrils, or the adventitia.

The earliest changes in the endarteritis, in an artery of the same calibre, stained by the same method, are to be found in the inner blue layer, or the intima (Fig. 4). Where only a small segment of the circumference is involved in the proliferation, the remainder of the intima may not differ from the normal; but approaching the proliferated part, the endothelial cells of the intima together with a thin strip of the blue layer are loosened from the underlying homogeneous-appearing part which always remains in close contact with the elastica. The presence of epithelioid cells and an occasional lymphocyte beneath the loosened part seems to indicate that they have pushed the intima inward. Proliferation of the endothelial cells rapidly increases the thickness of the layer. Increasing number of epithelioid cells lie between the intima and the elastica and push in among the proliferated fixed tissue cells. The cells of the intima at this point have the appearance of proliferating connective-tissue cells. They are spindle shaped, often branched, and the ends have a fringed appearance.

About these cells and interlacing among other elements of the proliferation are many blue-stained, connective-tissue fibrils. At the base of the intima there are other fibrils which are stained red or orange; for the most part these are coarser than the blue fibrils, but in a few places there are some that are more delicate and lie densely matted together. These latter red fibrils are probably fibrin.

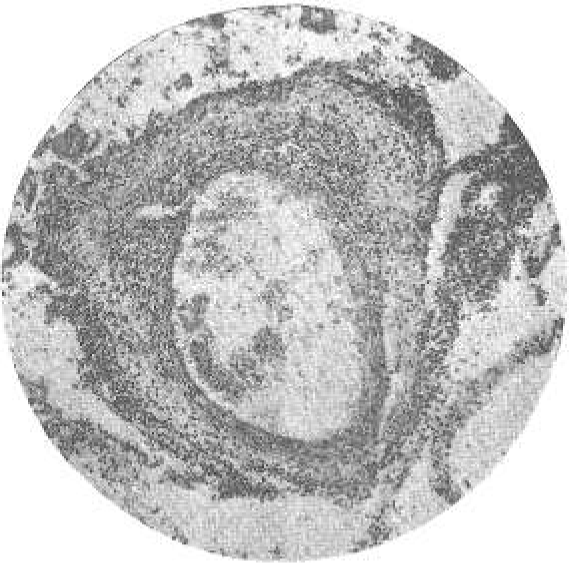
The infiltrating elements beneath the intima and in the proliferation are for the greater part epithelioid cells; where the intimal proliferation is slight and the layer compact, a few lymphoid nuclei occur beneath the intima, but where the proliferated cells are loosely arranged there are many epithelioid cells. In a few instances quite large focal aggregations of epithelioid cells lie between the intima and the elastica.

One artery, the intima of which shows extreme thickening, has a row of peculiar homogeneous masses, extending at least a quarter around the circumference. They lie deep in the proliferation near the elastica. The elastica, however, is plainly visible beneath in an apparently unchanged condition. These masses appear as confluent plaques of no characteristic shape. They stain brilliant red by Mallory's connective-tissue method, and deep blue with Weigert's fibrin method; these are apparently a degenerative product possibly of the newly formed connective tissue. Unfortunately there are no preparations which could determine whether or not they are of hyaline nature. Smaller amounts of this substance are present in a few arteries showing large proliferations of the intima. Close to this red area is a large, round, finely granular mass which remains unstained in all of the methods used.

The elastica in all preparations shows only slight changes. In some of the preparations by Mallory's connective-tissue method it is more of a yellow than a red color, and opposite these places the intimal proliferation is most marked. In a few instances there is splitting off of a few lamellæ from the inner border of the elastica, but there are no infiltrating elements beneath these and it is probably due to some irregularity in the sectioning of the vessel.

The media is not often involved. In a few arteries it is infiltrated with lymphoid cells; this occasionally amounts to small focal aggregations. Rarely one sees long-drawn-out cells as if they were migrating through the wall. The adventitia is more frequently affected than the media but less than the intima. The process is an infiltration and not a proliferation. In one artery which shows no trace of endarteritis there are lymphoid and plasma cells scattered through the adventitia. Those arteries showing the most marked proliferation of the intimal cells generally show the greatest adventitial infiltrations. One artery shows swelling of the nuclei of the adventitial cells; these are pale and have an invaginated margin; among them are scattered nuclei, which are much larger than the pale forms; often these have threads of chromatin grouped in their interior; one nucleus shows a mitotic figure. There are very striking differences between these two varieties of cells. Sometimes there is a band of lymphoid and plasma cells on the border between the media and adventitia.

FIG. 2.

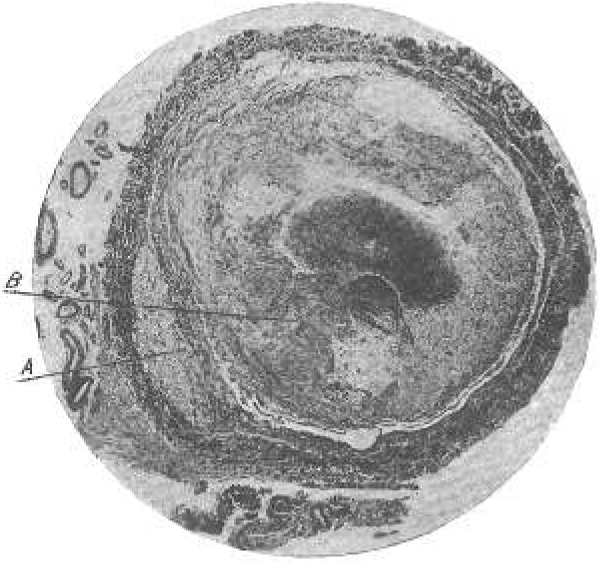


Vein in pia mater with swollen and infiltrated wall. Eosin-methylene-blue stain. Magnification 175.

A few of the larger arteries of the pia show at one point of their circumference a focal massing of polynuclear leukocytes, together with a few lymphoid and plasma cells. In most of these foci the form of the leukocytes is generally unchanged, but in some instances a focus is distinctly necrotic, the leukocytes staining poorly and their nuclei fragmented. In several arteries the necrotic focus is continuous with a similar focus in an adjacent vein. A number of these preparations were stained by methods for showing bacteria, and while in the débris there are scattered coccus-like particles, no significance can be ascribed to them, owing to the impossibility of here differentiating between organisms and nuclear fragments.

Veins. The veins of the meninges more generally show changes than the arteries. Commonly the larger veins are filled with red blood cells and relatively more polynuclear leukocytes than normal. In some there are threads of fibrin which in a few instances lie in masses near the intima. The adventitia is usually infiltrated and its fixed tissue cells are swollen; these two processes give the vessel a somewhat increased size (Fig. 3). The infiltration, which is much greater than in the arteries, is made up of lymphoid and plasma cells, with a few epithelioid cells. In a few veins the walls are necrotic and at these places are densely infiltrated with polynuclear leukocytes; some of these latter contain inclusions of necrotic débris. The necrosis is more extensive than in the arteries and extends from the adventitia to the intima, but seems to be more advanced in the outer part of the wall, while next to the intima the leukocytes are best preserved.

FIG. 3.

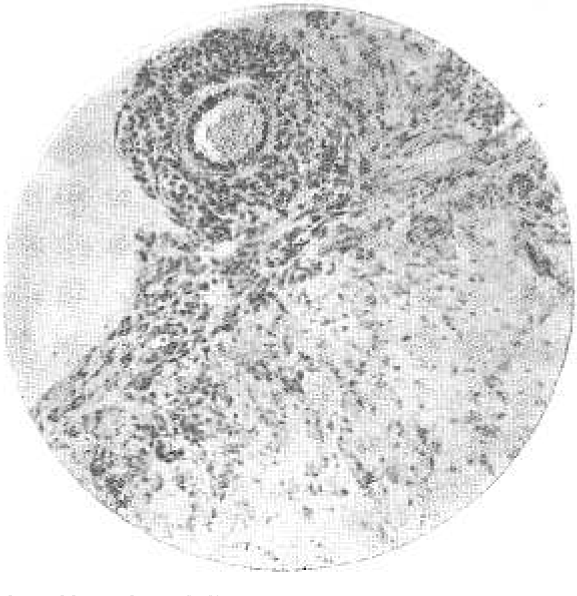


Middle cerebral artery. *A*, hemorrhage between media and adventitia. *B*, proliferated intima with adherent thrombus. Mallory connective-tissue stain. Magnification 30.

In the description of the meningeal exudate was noted the presence of a tumor-like mass, infiltrated with leukocytes, projecting from the adventitia of a vein (Fig. 1). The histological picture of this is not that of a gumma, but rather a focal massing of leukocytes at this point of the vessel wall, many of which have become necrotic.

In the gross examination of the brain, the left middle cerebral artery was thickened in its proximal part and was of a bluish-black color (Fig. 4). Sections across the artery at this point show great proliferation of the intima with a thrombus partially occluding its lumen. The proliferative changes in the intima are quite like those above described, excepting for some differences in the infiltrating elements; scattered among the proliferated intimal cells are many polynuclear leukocytes and epithelioid cells. These latter usually have inclusions of yellow pigment; in some of these are red blood cells which still preserve their normal outline yet will not stain with eosin. The greater number of these phagocytes lie deep in the intima, near the elastica. Adherent to the proliferated intima is a thrombus composed for the larger part of a fine, granular-appearing substance which stains poorly; in this are many branched fibroblasts and a few epithelioid phagocytes. In cross section the thrombus fills a little more than one-fourth of the lumen; the remainder of the space is packed with red blood cells, among which are fibroblasts and scattered small clumps of fibrin. There are a few epithelioid phagocytes with inclusions of yellow pigment or pale shadows of red blood cells. The media of this artery, excepting for a small segment, is of loose structure, and contains a number of infiltrating cells; some of these are long, compressed forms as if in process of emigration. The infiltration is very abundant at the point of attachment of the thrombus. At the point where the intimal proliferation is greatest there is a small hemorrhage between the media and adventitia, and both adventitia and media here show their greatest infiltrations; polynuclear leukocytes are quite numerous and often show necrosis.

FIG. 4.

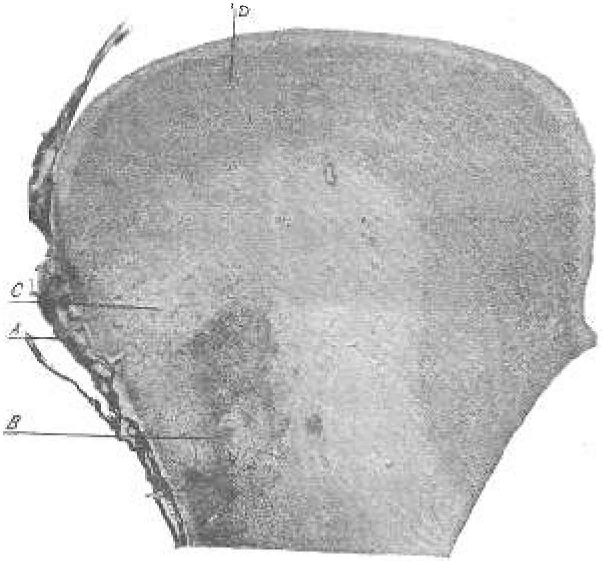


Hypertrophy and hyperplasia of glia cells in the superficial layer of the cortex. Adherent to the cortex is a piece of pia mater with a swollen and infiltrated vein. Nissl stain. Magnification 100

It seems best to describe the changes in the brain substance according as they are diffuse or focal.

As diffuse changes in contradistinction to focal are included, those changes in the brain substance occuring apparently independent of foci of encephalitis or hemorrhages. It is not possible to place sharp distinctions between the two processes, as diffuse processes show greater intensity at some points than at others. The diffuse process is characterized by degenerative changes in the nerve cells, and by degenerative and proliferative changes in the glia and vessels. No section of the many examined is free from changes, although in the majority they are very slight.

FIG. 5.



Frontal convolution. *A*, pia mater. *B*, area of encephalitis. *C*, bordering zone in which nerve cells have been destroyed and where glia and non-nervous elements show proliferative changes. *D*. comparatively uninjured nerve-cell layers. Nissl stain. Magnification 10.

Low Magnification. In most sections there is present a hypertrophy and hyperplasia of the glia cells of the superficial layer of the cortex. The degree of this varies greatly, at some points being more marked than at others. The progressive changes in not a few places are so great that the contrast between superficial layer and nerve cell layers is obliterated (Fig. 3).

Sections from regions but slightly changed show no disturbance of the normal cortical architecture. In regions severely altered there are patches from which the nerve cells have disappeared, and those which remain appear shrunken and severely diseased (Fig. 5).

In these latter regions the substance between the nerve cells is strewn with disintegration products of nerve cells and obscured by the swelling of the glia cells.

High Magnification. Sections from the regions least altered show only slight disintegration of the Nissl bodies of the nerve cells. Many nerve cells are quite normal.

In the more severely altered regions, such as those showing under weak magnification evidences of nerve cell destruction and disappearance, there are present a variety of changes in the nerve cells. Two of these changes are so characteristic and occur so frequently that one seems justified in regarding them as of especial importance in the general process present in the brain.

Among the nerve cells of such a region there are numerous dark, shrunken, angular forms, the apical process and dendrites of which are traceable a considerable distance from the cell body; the axone is similarly stained. Internally these cells present a fine, crumbly structure; no distinct Nissl bodies are to be made out; many cells appear to be filled with a fine, pale dust; others may be described as finely vacuolated or honeycombed. In a few cells no trace of cell structure lies between the nucleus and the cell wall. The nucleus is generally pointed; although in some of the cells the nuclear membrane is fairly well outlined, in the majority the membrane cannot be differentiated from the deeply stained homogeneous nuclear ground substance. The nucleolus has a tendency to assume irregular shapes.

Scattered among the nerve cells of such a region are dark-blue, homogeneous nuclei, about which lie pale granules; these are evidently end stages of cells destroyed in the above type of alteration. This type of change rarely is distributed all through a region, occurring only where the cortical changes are most severe. Among or not far from such cells commonly occur others showing an entirely different type of alteration. Forms quite similar to this type occur among the nerve cells persisting in or bordering foci of encephalitis.

In the second type of alteration the nerve cells are swollen; the dendrites and axone are traceable far from the cell; within the cell the granules have disappeared, leaving the cell body filled with a pale meshwork; this latter is sometimes so faintly visible that the cell has almost a homogeneous appearance. The nucleus usually presents a pale-blue, homogeneous appearance and its membrane is invisible. In a few instances the nucleus is indistinctly mottled. Frequently two or more coarse granules, staining an intense blue color lie within the nucleus. In some cells the nucleus becomes irregular in outline, and as the granules within the cell disintegrate it fades away. The nucleolus takes on a mulberry-like form. Ultimately all traces of the cell structure disappear. Not infrequently these cells show deeply stained particles of substance lying on or about the cell; sometimes these are massed at the base of the cell or at the tip of the axone. These are what Nissl regards as degenerations, and as incrustation upon the pericellular net.

This last type of alteration is not a common one. In no other cortex have we seen it in such numbers. It is a very severe condition and is always associated with various end changes of the same general type of alteration.

In addition to these two types of cell changes there are isolated examples of Nissl's "grave alteration," a type of alteration in which the body of the nerve cell breaks up into small characteristic ring-like degeneration products, the nucleus atrophies, and finally the entire cell disappears. There are a few cells which show the experimental axonal reaction; this is characterized by swelling of the cell with disintegration of the Nissl bodies, always more marked at one side of the cell. The nucleus, at the same time, takes a position close to the wall.

While the alterations among the nerve cells are varied and apparently all of a regressive character, the glia cells, excepting in a few places where the tissue injury is extreme, show progressive changes of a constant character.

There is a good deal of uncertainty as to just which of the nuclei present in the cortex are glia elements; there are, however, certain forms which are easily identified and which, in their progressive development, show constant characteristics in their transitions up to forms which are unquestionably glia cells.

The earliest stage in these progressive changes is swelling of the nucleus with an increase in size of its contained chromatin granules. At the same time there is noticed, spreading around the nucleus, a substance characteristic in its peculiar speckled or granular appearance. In the further development this substance becomes more compactly arranged about the nucleus and assumes the form of an oblong or oval cell body with radiating, process-like extensions; the nucleus takes an eccentric position, bulging from one side of the cell; gradually the granular appearance changes to one more homogeneous; from this stage the tendency is to shrink into what one regards as of the ordinary astrocyte type. This cell in some of its stages is probably the fibre-producing form. In satisfactory preparations there are increased numbers of glia fibres where these types occur, and it is often possible to demonstrate fibres still attached along the sides of the cell body or processes.

Progressive changes occur among some of the glia cells in the superficial layer of the cortex in every section examined. The intensity of these changes varies greatly; while generally the glia cells are rather evenly distributed through the superficial layer in any one section, there may be in the same section a focal increase of cells which sometimes fills the entire thickness of the layer (Fig. 3).

The glia cells of the superficial layer show more fully developed forms than those of the nerve cell layers, excepting where there are areas of severe tissue injury. The changes present in this layer appear to be intimately related to the changes in the pia mater. Where the meningitis is most intense there occurs the greatest reaction in the underlying glia cells, and where the meningitis is slight the glia reaction is not marked and is confined to the upper margin of the layer. Similarly, where there are areas of encephalitis lying in the more superficial part of the cortex there is always seen a marked glia hyperplasia.

In these areas of focal accumulations of glia cells, and where the glia cells have large cell bodies, it is always possible to demonstrate with elective staining methods that the glia fibres are also increased.

The glia cells of the nerve-cell layers show earlier and less intense changes than those of the superficial layer. No section is free from changes. In regions which show no foci of encephalitis the cell body is rarely completely developed, the cells showing the earlier progressive changes. Where the alterations in the nerve cells are slight, there occur swollen glia nuclei lying in a mass of delicately speckled protoplasm; sometimes these lie in groups of two or three. Where the nerve-cell changes are severe, and where the ground substance of the cortex is strewn with the débris of disintegrated nerve cells, the glia cells show the more advanced changes. There are a few places where the whole cortical structure shows severe injury, and in these there occur among glia cells showing progressive changes dark nuclei, which are apparently regressive forms of glia cells.

The distribution of the glia changes in the nerve-cell layers is peculiar. There is an unevenness in their distribution and a tendency toward focal variations in intensity. In a few areas where the nerve-cell changes are very severe, many cells having disappeared, the glia changes are very slight.

There occur in the cortex other forms of nuclei, the nature of which are not at all certain. One of these is a long, spindle-shaped cell, which Nissl calls a "Stäbchenzelle;" this is present in almost every region studied and appears as a long nucleus with coarse chromatin granules and filaments of cell-body substance projecting from either end. These cells will be described later.

Another form is the satellite nucleus; these are so few that they apparently play no part in the process present. There is one point which may be of interest, and one which is often illustrated in other processes, namely, that these satellite nuclei show no changes in regions where the glia nuclei show the most characteristic progressive alterations.

Other types of nuclei present in the nerve-cell layers are related to focal processes and will be described in that connection.

In general, it can be said that these changes in the glia cells are more delicate indications of the changes present in the cortex than are the changes in the nerve cells. In some regions where it is not possible to regard the nerve cells as altered, the glia cells show distinct though very early changes.

The white substance of the cortex shows these diffuse changes to a far less extent than the nerve-cell layers. Those changes which one finds in the glia nuclei are apparently always of a focal character, dependent either upon vascular lesions in their neighborhood or they are reactions secondary to foci of encephalitis in the overlying nerve-cell layers.

BLOODVESSELS. In the regions showing more or less diffuse alterations, two apparently different changes are seen in the bloodvessels. These two types are: 1. Infiltration of the vessel walls and perivascular spaces. 2. Swelling of the vessel walls.

1. *Infiltrations.* The vessels which extend in from the pia frequently have an extension of the pial infiltration into their walls and perivascular spaces. The distribution of these infiltrated vessels is peculiar; they occur in regions showing only slight changes in the cortex and in the neighborhood of vessels showing no infiltrations whatever. Rarely do they extend deeper than the upper nerve-cell layers. They are most common in the superficial layer at the bottom of a sulcus.

The infiltration in and about a vessel wall is never very great. Generally there are only a few nuclei present. In this infiltration there occur lymphoid and plasma cells, epithelioid cells, with inclusions of pigment, and rarely a mast cell. These cells lie in the adventitia and perivascular space. Sometimes lymphoid cells alone are present, and sometimes only plasma cells, more generally the two occurring together.

Occasionally there are infiltrations of the walls of vessels lying deep in the nerve-cell layers and which show no connection with the pia, at least, not in the plane of the section studied; there is no uniformity in the distribution of these vessels.

In no way can it be seen that these infiltrations differ from those associated with general paralysis, either in the character of their constituents or in their localization in the vessel walls. In most cases of general paralysis, however, the infiltrations are larger, but there often are cases in which they are not more marked than here.

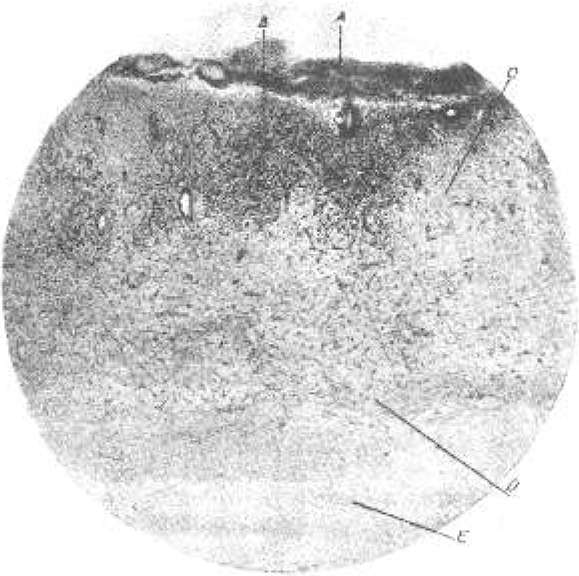
2. *Swelling of the Vessel Walls.* This is a change present in varying intensity in every region studied; it is always less marked where the changes in the nerve cells and glia are slight and is greatest where these are most severely altered. As this process is nowhere as marked as in the lesions of focal encephalitis, it will be better to describe it later on in that connection.

FOCAL CHANGES. As focal changes, there occur in the brain: 1. Areas filled with the elements characterizing granulation tissue or areas of encephalitis. 2. Changes of simple necrosis or softening, directly related to a vessel in their immediate vicinity. 3. Hemorrhages. 4. A few foci, which, from their compactness and similarity to the histological picture of a gummatous tumor, are so regarded.

In all of the focal processes it is necessary to discriminate between the primary process and various reactive changes in the elements bordering the focus. It is difficult to judge as to the relative or absolute number of these various focal processes. In the fresh brain it was not possible to identify the smaller foci, but after hardening in formalin many were picked out from their more or less marked contrast with the surrounding tissue.

As encephalitis we here describe a process characterized by death of the nervous elements proper, proliferative changes in the vessels, and an infiltration of the area with epithelioid cells. Accompanying this process there are always reactive changes in the glia. The area is separated from regions in which the elements, while not normal, preserve much of their integrity by zones in which the elements show reactions differing according to their distance from the focal process.

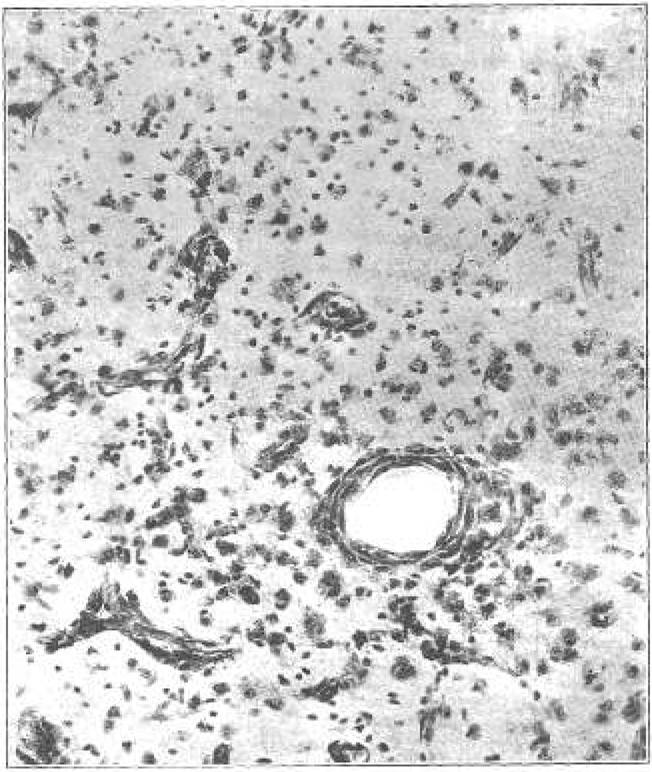
FIG. 6.



Area of encephalitis. *A*, infiltrated pia mater. *B*, focus of granulation tissue. *C*, zones in which glia and non-nervous elements are proliferating. *D*, layer of epithelioid cells lying along the edge of (*E*) white substance. Nissl stain. Magnification 15.

It is not demonstrated that any of the foci are direct invasions of the process from the pia mater. In some instances, while the infiltration of the pia mater and that of the underlying cortical substance appear to merge into each other, on careful examination a difference between the two processes is seen. This is principally in the character of their elements. In the pia the predominating cell is the lymphocyte, while in the underlying cortex it is the epithelioid cell which occurs in greatest numbers, lymphocytes being quite rare. The upper part of the superficial layer of the cortex contains strikingly fewer cells than the regions on either side and forms a boundary zone between the dense infiltrations of epithelioid cells below and the meningeal exudate above.

FIG. 7.

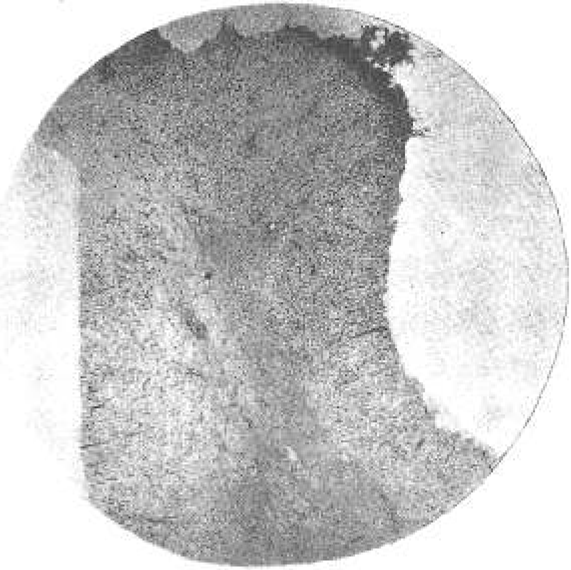


Epithelioid cells and swollen vessels from the outer edge of encephalitis area. Nissl stain. Magnification 225.

Each of the larger foci of encephalitis is limited primarily to the nerve-cell layers of the cortex. In some instances it involves all of the layers; in others its upper level reaches the position of the layer of small pyramidal cells. (Figs. 6, 7, 8.)

In the earlier stages of the process these areas of encephalitis are separated from the white substance by a border of closely packed epithelioid cells. Later this sharp demarcation is less prominent. The focus is bordered on either side by zones in which there is a reaction differing in intensity according as they lie close to or removed from the focus. One of these foci, under low magnification, shows the normal cortical architecture entirely changed. Nerve cells are not to be distinguished, and the area is filled with swollen vessels and pale cellular elements (Fig. 7). Under the immersion objective not a normal nerve cell can be seen. Here and there lie dark cells, which, from their general appearance, seem to be the remnants of former nerve cells; such also are scattered, shadow-like pyramidal forms, which have a faint yellow tinge.

FIG. 8.



Frontal convolution, the entire area showing encephalitis with almost total destruction of nerve elements. Nissl stain. Magnification 15.

Most striking in one of these foci are the swollen bloodvessels and the large numbers of epithelioid cells crowding the area. All of the bloodvessels are swollen; as their individual cells increase in size and become broader, their protoplasm has a tendency to stain deeper. In some cells the protoplasm has a granular appearance and is usually more dense at one pole of the cell; this part of the cell stains an intense blue color in Nissl preparations. The nucleus increases in size; its interior has a glassy, homogeneous appearance and rarely is it possible to distinguish the chromatin network. The nucleolus is large and of a characteristic blue color; often its outline is oblong or otherwise irregular; occasionally there are from one to three small, deeply stained granules scattered around the nucleolus.

This swelling of the cells of the walls gives the vessel a laminated appearance. It occasionally seems as if the vessel is a mere nest of concentrically arranged cells. The lumen is almost obliterated; sometimes a leukocyte or red-blood cell is pushed in among the cells of the walls. The normal compact structure has become loosened and the cells are pushed apart. Some vessels cut in their long direction seem as if their walls are split into two layers. A few of the cells show mitosis. The relation of these swollen cells of the vessel wall to the epithelioid cells abounding in their neighborhood is interesting. In the process of swelling some of the outer cells of the wall become loosened at one end; this end is often noticed projecting free from the wall. While the cells which belong positively to the vessel wall are compact and lack the spongy or vacuolated appearance of the free epithelioid cells, it is common observation that as soon as a cell shows indications of loosening from the wall of the vessel its protoplasm appears less compact. It seems quite possible to trace all stages between the swollen cells of the outer parts of the vessel wall and the epithelioid cells lying free in their neighborhood.

It is notable that the epithelioid cells are most numerous near those vessels which are most swollen; while around the vessels in the peripheral parts of an area of encephalitis they are not found in large numbers. Some of these swollen vessels, notably the larger, have lymphoid and plasma cells crowded in among the cells of their walls, and in places appear quite the same as the infiltrated vessels in other parts of the cortex where the tissue injury is less marked. From the study of this and similar foci, it seems as if the swelling of the walls and infiltration are two separate processes, the latter process being more chronic.

The epithelioid cells crowding the focus of encephalitis for the most part do not differ from those found in the areas of inflammation of other organs. They are the "Körnchenzellen" of German descriptions and correspond to the cells which abound in the early stages of anæmic softening of the brain. There are some cells present in considerable numbers which show a great variety of form; the body of these cells is sometimes long, with branching protrusions from one end, or a part of an irregular-shaped body may be extended like the pseudopod of an amœba. These cells are always coarsely vacuolated; in some there are yellow-tinged inclusions; many have large spaces, like digestion vacuoles. What these cells are is difficult to decide.

Another type of cell occurs in few numbers in the central part of the areas of encephalitis, but is very numerous in the bordering regions. About one of these foci it is distributed in ill-defined zones, in each of which it shows phases of development different according as they are near or far from the parts showing the more severe general tissue changes. In regions more or less removed from areas of encephalitis, where only slight general changes are noticed in the nerve cells and glia, there occur scattered in few numbers long pale nuclei, with a rather indistinct, filament-like cell body extending from either end. These nuclei are oblong or fusiform; in Nissl preparations they stain more of a greenish color than the ordinary glia nuclei and contain a number of coarse chromatin granules. The cell-body substance is slight in amount and finely granular in structure. In this stage it corresponds evidently with what Nissl describes as the "Stäbchenzelle," a form occurring frequently in the cortex of general paralysis. Nearing the focus of encephalitis there is an increase in the number and size of these forms; they have become longer and broader; the cell body is coarsely meshed and vacuolated; along the edge of a focus of encephalitis there are branched forms, apparently of the same element; the cell wall is here sharper outlined; the nucleus appears to be placed nearer to one side, and the cell body becomes more loosely partitioned and seems to be in a process of channelling through. Often two or more will be joined at their ends or at the tip of a branch. In a few instances it seems as if they are directly connected with the wall of a delicate vessel. It is difficult to decide what the origin and function of this type of cell are. The cells differ in so many ways from glia elements that it seems certain that they are not of this class. They are also not of the type of the common epithelioid cell. There are evidences that they are related to the process of forming new vessels, but no positive conclusions can yet be stated. We have seen this form and the large branched vacuolated phagocyte cell in simple encephalitis after trauma, and the former is not uncommon in various organic brain diseases, notably general paralysis, where the formation of new vessels is often quite prominent.

Other cellular elements present in one of the foci of encephalitis are glia cells in various progressive stages. Most of these show hypertrophy of the cell and nucleus. The nucleus is large, containing coarse chromatin granules and lying at a corner or side of a more or less homogeneous cell body, from which project short, stubby processes. In these foci the glia cells are always fewer than in the bordering regions; in the older parts of the focus the glia cells are shrunken and present the form of the common astrocytes.

Scattered through the focus are various nuclei difficult to identify; some are like the lymphoid nuclei occurring elsewhere. Many are nuclei apparently regressively altered. In preparations by Nissl's method these appear as dark-green nuclei of irregular outline, and usually of a homogeneous structure; in some it is possible to distinguish a few dark granules. Polynuclear leukocytes are very rarely seen.

The areas of encephalitis are bordered by zones which show changes different from those present in the area itself, and are a combination of the changes which we have described as diffuse and those caused by reaction secondary to the encephalitis (Fig. 6, c).

Each focus is bordered by a zone in which nerve cells are few;

great numbers of them have disappeared, and those remaining are in various regressive changes leading to complete destruction of the cell.

The vessels are swollen and show proliferative changes, which are, however, never as prominent as in the focus itself. Many show the adventitial infiltrations seen all through the cortex. In this zone lie large numbers of the peculiar long cells described earlier. Epithelioid cells are few and lie close to the margin of the focus and always alongside of a vessel. Hypertrophied glia cells are numerous; these have swollen nuclei, always of a characteristic glassy appearance, and differing in this stage from all the other nuclei present; the nucleus contains one or more coarse lumps of chromatin; surrounding the nucleus is a protoplasmic body; in the greater number of cells in this zone this appears as a large, bulging, homogeneous mass with short, stubby processes. In the older of these the border seems to take a deeper stain than the rest of the body. This type represents the fully developed hypertrophied cell, and between this and the earlier progressive changes there are all stages. Some of these cells have two nuclei; none show mitosis. There are a few glia cells occurring in places where the tissue injury is most severe, which have swollen, loosely-meshed cell bodies, which stain poorly; occasionally there are the peculiar forms of glia which Nissl calls "Gliarasen." These are "mould-like" masses of spreading protoplasm, in which lie clusters of glia nuclei.

The white substance of those regions where the cortex shows focal encephalitis has hypertrophied glia cells close to the focus. Only one region, and this where several foci are in one section, shows diffuse changes throughout the white substance. In this region hypertrophied glia cells are scattered everywhere. There are also many of those shrunken, dark, homogeneous nuclei described earlier as occurring in the focus itself. Epithelioid cells occur in moderate numbers. Close to the focus there are swollen vessels and delicate, newly formed capillaries.

In general, the vessels of the white substance are less altered than those of the nerve-cell layers. Occasionally there are infiltrations of lymphoid and plasma cells in their walls.

2. Areas of anæmic necrosis due to vessel changes—*i. e.*, simple softenings. Apart from the areas of encephalitis, there are several regions which show the characteristic process of softening; these lie always in the course of the vessel, visible in the plane of the section. They are only seen along the deep or medullary arteries. One such focus of softening borders an artery extending through the nerve-cell layers into the white substance; around the vessel the tissue is of loose structure and infiltrated with epithelioid phagocytes. Formalin-fixed preparations stained with Scharlach R. show that these cells are crowded full of fat or myelin granules. The glia bordering these areas of softening always shows progressive changes. In a

number of places away from the foci of tissue injury the epithelioid cells in the adventitia or perivascular infiltration contain granules giving the reaction of fat.

3. *Hemorrhages.* There are no focal hemorrhages in the cortex. In the left internal capsule and in the left thalamus there are small punctate hemorrhages. Among the pyramid fibres in the right side of the pons there are a number of larger hemorrhages. Several smaller hemorrhages are present in the medulla. The nuclei of the ninth and tenth nerves on both sides are infiltrated with blood. In all of these regions the bloodvessels are intensely engorged; some of these are ruptured and their neighborhood is infiltrated with blood cells. Around one of these hemorrhages in the medulla the tissue is porous, such as occurs in early softening, but there is no demonstrable reaction of the fixed tissue cells. Always near these areas there are many round-shaped or irregular-shaped myelin bodies; there are no epithelioid phagocytes. The red cells have their forms well preserved and stain deeply with eosin. These facts seem to show that the hemorrhages present are very recent.

4. *Foci Resembling Gummatous Tumors.* Excepting for the focus of necrosis noticed in the walls of some of the meningeal vessels, there is nothing resembling a gumma in the brain above the medulla.

In the medulla there are several foci which in their histological picture correspond to gummata and differ essentially from the other focal processes described. One of these is in the pia around the root of one cochlear nerve. Here there is a focal accumulation of densely packed epithelioid-like cells, with many polynuclear leukocytes in the central part. The area stained poorly; many of the cells show characteristic necrosis. The mass of cells spreads into the pia along the course of the nerve and many push in among the nerve fibres.

A section passing through the lower part of the olive shows five small focal cellular accumulations in the gray substance around the central canal. These are composed of closely packed cells, having pale nuclei with coarse chromatin granules. These nuclei are of a variety of shapes; some are oval, or flask-shaped, or sharply bent at their middle. Most of the nuclei are bordered by a broad rim of protoplasm. These cells differ from those of the infiltrations of the vessel walls of this region; these latter always resemble lymphoid and plasma cells, while those of these foci are of the type of epithelioid cells. It seems probable that these are specific gummatous tumors.

Medulla and Spinal Cord. The pia shows an infiltration differing only in intensity from that of the convexity of the brain. Vessel changes are, however, more general. The majority of vessels are engorged with blood. Many have perivascular infiltrations; many show proliferative changes in the intima and adventitia. One artery in the region of the medulla has endarteritis and occlusion of its lumen by a partially organized thrombus. A few vessels show areas of necrosis in the media and adventitia similar to those found in the meninges of the brain. It is not demonstrable that the meningitis is more marked at any special level of the cord further than that where the nerve roots are most abundant and the pia of loosest texture, as in the lumbar and sacral levels, the meningitis is more prominent than in other regions.

The walls of the vessels in the medulla are more generally infiltrated than those of the brain. Not only the vessels extending in from the pia, but those lying deep in the more central parts show larger accumulations of lymphoid and questionable plasma cells in their walls and perivascular spaces. The focal hemorrhages occurring here have been noted. Along almost the entire length of the medulla and cord the glia cells of the margin are hypertrophied. At one point there is a triangular area of hypertrophied glia cells extending deep into the medulla. There are no signs of an inflammatory process in this area.

Satisfactory preparations of the cord by Nissl's method show remarkably well-preserved nerve cells. Besides the hypertrophy of the glia cells around the margin there is a slight degree of infiltration of cells from the pia around the arteries and posterior root fibres.

In a section through the cervical cord there are present two small foci in the gray commissure in which the glia cells are hypertrophied.

Many sections from the medulla and cord prepared by methods for demonstrating the myelin sheaths show no fibre degenerations. Marchi preparations show scattered, blackened fibres among others which appear normal. These latter findings are so uncertain that they are not regarded as important.

Fibre Degenerations of the Cortex. Preparations were studied from many different regions, but only one of those shows any coarse fibre degenerations. This was from the left gyrus rectus (Fig. 9).

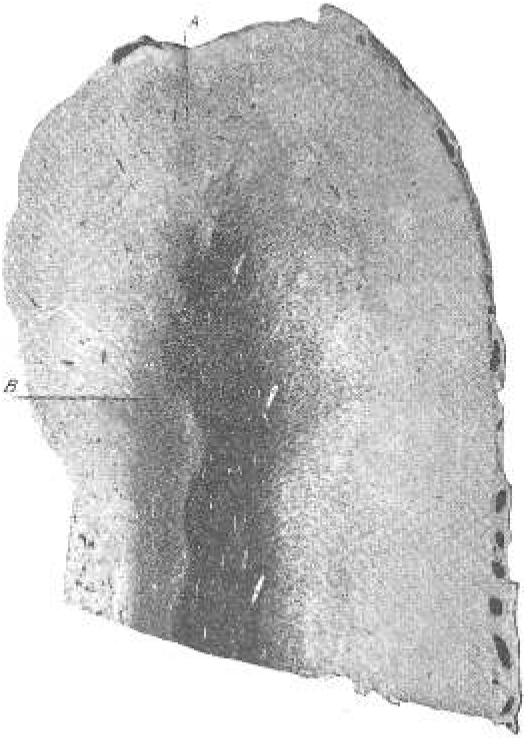
Even without magnification, there is noticeable a striking paleness of part of the white substance. When more highly magnified, the degenerated part appears to involve about a third of the white substance.

It is clearly demarcated from the normally stained part, but from this latter there passes into the degenerated part some fibres, either singly or in sprays, which are well preserved. The degenerated portion is made up of pale, barely visible fibres, among which are scattered a few that are well stained. It is easy to find evidences of degeneration among the fibres along the edge of the more normal part, principally flask-like bulgings of the fibres; these are also present in those stained which lie scattered through the degenerated area. In this section there are present in the nerve-cell layers two small and one larger area in which the nerve fibres are absent; each of these is bordered by fibres relatively as numerous as in other regions at this depth. Each of the areas show severe general tissue changes, and contain dark nuclei and an increased number of capillaries, which are much engorged. In every way these agree with foci of encephalitis, as seen in more suitably prepared sections.

Above on either side of these areas there is a very distinct thinning of the tangential fibres. The larger of these foci lies directly above the part of the white substance from which the fibres have disappeared. Between the focus and the white substance only a few pale, radiating fibres remain.

While this is the only region which shows coarse changes, several others show finer degenerations.

FIG. 9.



Gyrus rectus. The fibres in the left half of the white substance degenerated. *A*, focus ot encephalitis. *B*, area of fibre degeneration. Myelin sheath stain. Magnification 10.

In the right frontal convolution the tangential fibres of the superficial layer are in places reduced to a few isolated fibres, and at some points are entirely interrupted. In these defective places there is always noticed hypertrophy of the glia cells. The pia at this point also shows an intense infiltration. In this section, as in all of the others, it seems true that in this layer where the glia cells are hypertrophied the superficial tangential fibres are fewest.

In the left first frontal convolution there is a similar disappearance of the tangential fibres in the superficial layer. The same is true of the left and right anterior central convolutions. In the occipital regions no change is noticed in the fibres.

In analyzing the case the early occurrence of the disease of the nervous system is of clinical interest. In many of the text-books it is stated that syphilis of the nervous system is a phenomenon occurring late in the disease. There have, however, been a number of analyses of large series of cases, notably by Naunyn,[1] Gowers,[2] and Hjelman,[3] as well as a number of isolated cases, which show that syphilis of the nervous system often occurs within a few years or even within the first six months after infection (Oppenheim[4]). In our case the first nervous symptoms occurred within six months, and the entire course was completed in eight months after infection.

Anatomically, syphilitic disease of the central nervous system may manifest itself as: 1. Gummata. 2. Chronic hyperplastic inflammation. 3. Disease of the bloodvessels. To these may be added the parasyphilitic processes, such as those of tabes and general paralysis. It is not uncommon for all of these three to be present at the same time, and multiformity is quite characteristic of syphilis of the nervous system. This is notable in the present case.

In this case the most striking anatomical changes are those of the bloodvessels, while the production of focal gummata forms only a minor part of the process. In most of the reported cases of early syphilis of the nervous system lesions of the bloodvessels are more marked than focal gummata. Kahane[5] states that the diseases of the brain which occur in the early period of syphilis have the common anatomical character of almost always involving the bloodvessels, while gummata in the central nervous system, as well as in other organs, tend to occur late in the disease.

The meningitis present is a diffuse process and shows only a few questionable characteristics which would entitle it to be classed as a gummatous meningitis, the form which syphilis of the pia mater usually takes.

In its distribution and in the character of its elements it shows nothing specific. The great predominance of lymphoid and plasma cells and the rarity of polynuclear leukocytes give it the character of a chronic inflammation. These same elements are those which make up the meningeal exudate in general paralysis. It seems probable that the lymphoid and plasma cells appear first in the meningeal exudate, and that the occurrence of epithelioid cells and the few polynuclear leukocytes are related to differences in the severity of the tissue injury or of focal lesions of the coats of the bloodvessels. These latter cells are always found near vessels or where the exudate is in such quantity and the fixed tissue elements injured to such a degree that it is impossible to judge as to the source and the relation of the various cells to the primary process.

So far as can be determined, the cellular elements of the exudate differ little from those occurring in tuberculosis of the meninges; they, however, differ essentially from those of the acute infectious meningitides.

The intergrading forms of lymphocytes and plasma cells are interesting as showing the apparent close relationship of these elements.

Lesions of the bloodvessels are the commonest constant finding in syphilis of the central nervous system. According to Nonne,[6] they are seldom absent. Of the lesions, the endarteritis is the most familiar. In this case it is possible to study the process in an early stage. The first demonstrable step in the endarteritis is the lifting of the intimal endothelium by cells which pass in between the intima and elastica; the intima proliferation is secondary. Where these infiltrating elements came from was not determined. It is probable that they have wandered in from the adventitia, which in almost every instance shows local inflammatory changes. It is striking, however, how little the media is involved, as only rarely is it infiltrated, or can cells be seen which are in process of migration. The necrotic changes are always in the outer wall and spread from there inward. This necrosis is not unlikely the result of changes in the nutrient vessels of the adventitia. These findings accord with the position of Köster,[7] Friedländer,[8] and perhaps the majority of investigators, who regard the process as one spreading from the nutrient vessels toward the intima and do not regard the process as specific for syphilis; on the other side, Heubner[9] described the proliferation of the intima as the primary change due to direct action of the infectious agent of syphilis, the changes in the outer walls being secondary.

The thrombosis of the middle cerebral artery is apparently very recent. The intimal proliferation is not seen in the veins, but commonly there is present a mesophlebitis or periphlebitis. In the veins it is certainly noticed that the inflammatory process spreads from without toward the inner coat.

The pathological process in the brain and cord is characterized by multiformity. In the brain there is present a diffuse degenerative process affecting the nerve elements, glia and bloodvessels throughout the whole cortex. Apart from this, there are disseminated areas of encephalitis; these latter are apparently not dependent upon changes in the meninges. They show the phenomena of early granulation tissue, as well as local degenerative changes in the nervous elements and secondary reactive changes in the glia.

The hemorrhages, focal softenings, and the questionable gummata present are processes independent of these areas.

In its entirety the process may be classed among the few described cases of disseminated syphilitic encephalitis, as the inflammatory nature of the process seems to be the most prominent feature.

The frequent involvement of the meninges with lesions of the brain tissue has given the name meningo-encephalitis to a variety of syphilitic processes of the central nervous tissue. In the strictest use of the term, it has been applied to those processes where the inflammation spreads into the brain tissue along the bloodvessels from the meninges. In some instances it has been given to cases where there was present a meningitis with a gliosis of the underlying adjacent brain tissue; in others where a meningitis was associated coincidently with a process of simple softening. Apart from these, there are a few cases in which, in addition to a meningitis, there is present an independent inflammatory process in the brain tissue.

There is a good deal of confusion in the conception of encephalitis, and it is difficult to interpret many descriptions in the literature. This is true not only of syphilis, but of other brain diseases. The term encephalitis has been commonly applied to lesions which are those of an anæmic necrosis or simple softening. In other instances the description is that of a gliosis rather than an inflammatory process.

One is justified in regarding the process as one of syphilitic encephalitis where there occurs in syphilitic brain disease inflammatory phenomena in the brain substance independent of gummata, and not secondary to hemorrhages or the necrosis due to vascular obstruction.

Heubner,[10] in 1876, found, among some 150 cases of syphilis of the nervous system, 36 cases in which the process was regarded as one of simple inflammation. A careful analysis of 22 of the best of these descriptions convinced him that there was not a single case up to that time which could be regarded as a simple inflammation independent of a new-growth. In none of these cases was the histological examination thorough. In a few cases the inflammation might be ascribed to softenings in the neighborhood of a focal gumma overlooked during the examination. In many the inflammation was associated with meningitis. The remaining must be described as due to vessel disease, not focal.

It has not been possible to review all of the cases described as syphilitic encephalitis since Heubner's work. Many of the descriptions of the histological findings are incomplete, or no distinction has been made between the process of softening and that of an independent encephalitis. In others the phenomena of focal encephalitis are either described as extensions from the meninges or differ in essential ways from the case we have described.

A classical case often quoted in the literature is that of Charcot and Gombault,[11] in which there was present, in addition to focal gummata, independent areas of chronic inflammation. In the monographs of Bechterew[12] there are descriptions of a few cases which are regarded as encephalitis, independent of meningitis.

The best of these descriptions are cases of Oppenheim, Jürgens,[13] and Bechterew. In Oppenheim's case there was a focus of inflammation about 1 cm. in diameter in the pons and posterior corpora quadrigemina; the brain arteries were normal, and he designates the case as one of encephalitis.

Jürgens has described a case in which at death there were signs of secondary encephalitis. At the autopsy there was found an acute universal encephalitis. He regarded the disease as exceedingly rare.

The most complete description we have found is a case of Bechterew's.[12] This case in its histology resembles our own case very closely. The course was somewhat longer. The first symptoms developed in the year following infection, and death occurred two years later. He names the case one of disseminated syphilitic focal sclerosis, and adds that it is the only case of this type which has been completely studied, both clinically and pathologically.

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SOME OBSERVATIONS ON THE EFFECT OF ALTERNATING CURRENTS OF MODERATE FREQUENCY ON DOGS.

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The extensive and accurate researches of Prevost and Battelli[1] leave little to be investigated as to the effects which follow, and the cause of death from the application of commercial electrical currents to animals. We think it desirable, however, that we place on record

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[1] Journal de physiologie et de pathologie générale (1) 1899, tome i. p. 399; (2) p. 427; (3) p. 689 (4) 1900, tome ii. p. 755; (5) 1901, tome iii. p. 1085; (6) p. 1144.